

DEC 10 1998

Approval Date: _____

FREEDOM OF INFORMATION SUMMARY

ANIPRYL® (selegiline hydrochloride) Tablets
for use in dogs

NADA 141-080

Pfizer, Inc.
Groton, CT 06340

NADA 141-080

FOIS 1

Freedom of Information Summary

ANIPRYL® TABLETS

Table of Contents

<u>Section</u>	<u>Page</u>
1. <u>General Information</u>	1
2. <u>Indications for Use</u>	1
3. <u>Dosage Form, Route of Administration and Recommended Dosage</u>	1
4. <u>Effectiveness</u>	1
5. <u>Safety</u>	12
6. <u>Human Safety</u>	14
7. <u>Agency Conclusions</u>	14
8. <u>Labeling</u>	14

1. General Information:

NADA Number: 141-080

Sponsor: Pfizer, Inc.
812 Springdale Dr.
Exton, PA 19341

Generic Name: selegiline hydrochloride, the levorotatory form of deprenyl HCl

Trade Name: Anipryl®

Marketing Status: Rx: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Effect of Supplement: This supplement changes the original approval by adding a second claim for use in cognitive dysfunction syndrome at a new dose of 0.5-1.0 mg/kg.

2. Indications for Use:

Anipryl® tablets are indicated for the control of clinical signs associated with canine Cognitive Dysfunction Syndrome (CDS).

3. Dosage Form, Route of Administration, and Recommended Dosage(s):

The recommended dosage for oral administration for the control of clinical signs associated with cognitive dysfunction is 0.5 -1.0 mg/kg once daily, preferably administered in the morning. Initially, dogs should be dosed to the nearest whole tablet. Adjustments should then be made based on response and tolerance to the drug.

4. Effectiveness:

CD/HT- Study of Anipryl Effects on Cognitive Dysfunction in Aged Dogs

Type of study: Phase 1 - Placebo controlled, multi-site, dose range clinical field trial
Phase 2 - Open label, dose confirmation study

Investigators:

Investigator Name	City	State
Dr. Kimberly Anderson	Redford	MI
Dr. Tim Anderson	Bakersfield	CA
Dr. Joan Antle	Lyndhurst	OH
Dr. Gari-Anne Austin	Lawrenceville	GA
Dr. Richard Austin	Kissimmee	FL
Dr. Susan Baker	West Palm Beach	FL
Dr. Megan Bamford	Covina	CA
Dr. Glen Baron	Matthews	NC
Dr. Mildred Bass	Farragut	TN
Dr. Pete Beeman	San Francisco	CA
Dr. Lark Behrens	Tucson	AZ
Dr. James Bianco	Ardmore	PA
Dr. Gwen Bilyk	Saint Louis	MO
Dr. James Blackert	Sugarland	TX
Dr. Julie Bobb	Lexington	KY
Dr. Diana Bochenski	Buellton	CA
Dr. Leanne Brandt	Salt Lake City	UT
Dr. Rosemary Branson	Blythewood	SC
Dr. J.M. Brechin	Destin	FL
Dr. Brian Brock	Marianna	FL
Dr. Barbara Bucki-Ohm	West Coxsackie	NY
Dr. Colin Bullmore	Hamlin	PA
Dr. Colleen Calderwood	Rockville	VA
Dr. Karen Campbell	Bellevue	NE
Dr. Catherine Cannella	Fairfield	CT
Dr. Richard Caputo	Dearborn Heights	MI
Dr. Anthony Castrignano	Springfield	VT
Dr. Charles Chase	Cherry Hill	NJ
Dr. Ruth Chodrow	Staunton	VA
Dr. Philip Coccari	Oakdale	NY
Dr. Lori Coles	Salisbury	NC
Dr. Kimberly Collett	Alliance	NE
Dr. Bruce Coston	Woodstock	VA
Dr. Colleen Coyne	Des Moines	WA
Dr. Brad Craig, Jr.	Winston Salem	NC
Dr. Gerald Crawley	Mukwonago	WI
Dr. Julia Cummings	Walnut Creek	CA
Dr. James Cupp	Kansas City	MO
Dr. Leighann Daristotle	Lewisburg	OH
Dr. Paul Davis	Hanover	MA
Dr. Nancy Delaney	Fishkill	NY

Freedom of Information Summary

Page 3

Investigator Name	City	State
Dr. Don Dinges	Leawood	KS
Dr. Eva Divita	Port Richey	FL
Dr. David Dorn	Pittsburgh	PA
Dr. Coleen Dossey	Pleasanton	CA
Dr. Paul Drewry	Ludington	MI
Dr. Dennis Dugger	Oklahoma City	OK
Dr. Steve Dullard	Mendota	IL
Dr. Jon Duncan	Eugene	OR
Dr. Carol Eklund	Boise	ID
Dr. A. Susan Elkins	Hanover	PA
Dr. Peter Farrell	Alexandria	VA
Dr. Thomas Favale, Jr.	St. Charles	IL
Dr. Susan Ferraro	Chicago	IL
Dr. Jo Fisher	Bradley	IL
Dr. Arnold Fleisher	Hempstead	NY
Dr. Molly Foley	West Chester	PA
Dr. Leeann Foster	Los Alamos	NM
Dr. Joni Freshman	Colorado Springs	CO
Dr. Luke Fry	Lenexa	KS
Dr. Patricia Funnell	Ft. Wayne	IN
Dr. Orlando Garza, Jr	El Paso	TX
Dr. Alan Gassel	Farragut	TN
Dr. Elizabeth Gatti	Hadley	MA
Dr. Thomas Geiselhardt	Englewood	CO
Dr. Deborah Germeroth	Colorado Springs	CO
Dr. Brian Ghere	New Orleans	LA
Dr. Ann Goldhammer	Glendale	AZ
Dr. Norman Goldstein	Manlius	NY
Dr. Patricia Grant	Marina	CA
Dr. Jonathan Grant	Shokan	NY
Dr. Marthina Greer	Lomira	WI
Dr. Rick Grgurich	Emmaus	PA
Dr. Thomas Haig	Minden	NV
Dr. Marc Hardin	Overland Park	KS
Dr. Mike Harter	Rockford	IL
Dr. Cathy Hartney	Bayfield	CO
Dr. Lisa Hatfield	Phoenix	AZ
Dr. Kathi Heiber	Mahopac	NY
Dr. Nan Henderson	Durham	NC
Dr. Deirdre Hensen	Patchogue	NY
Dr. Chad Higgins	Cridersville	OH
Dr. Kathy Hinkle	Rohnert Park	CA
Dr. Leslie Hirsch	West Roxbury	MA

Investigator Name	City	State
Dr. Robert Hirt	East Aurora	NY
Dr. Christopher Holenstein	Gresham	OR
Dr. Keith House	Paris	TX
Dr. Kaaren Howe	Wayzata	MN
Dr. Eric Hudson	Brick	NJ
Dr. Susanne Hughes	Durham	NC
Dr. Laura Hulsey	Jackson	WY
Dr. Keith Huston	Mentor	OH
Dr. Curtis Ish	Hamburg	NJ
Dr. C. Gordon Jewett	Spokane	WA
Dr. Robert Johnson	Berryton	KS
Dr. Marcy Keefe	Brookfield	WI
Dr. Nancy Kelso	Charlottesville	VA
Dr. Jay King	O'Fallon	MO
Dr. Nicki Kominek	Dixon	CA
Dr. Harold Krug	Dallas	TX
Dr. David Kuykendall	Birmingham	AL
Dr. David Langford	Hollywood	MD
Dr. Melanie Lavergne	La Place	LA
Dr. Christina Leone	Oakwood	GA
Dr. James Lindley	Tempe	AZ
Dr. Jean Lindley	Miles City	MT
Dr. Jim Lofgren	Greensboro	NC
Dr. Reid Loken	Acton	CA
Dr. Patricia Luttgren	Lakewood	CO
Dr. Candace Major	Dallas	TX
Dr. Chris Mangini	Woodstock	VT
Dr. Ken May	Melrose Park	IL
Dr. K. Sue Mc Dougal	Pensacola	FL
Dr. Nancy Mc Gregor	Grove	OK
Dr. Michael McCreight	Seminole	OK
Dr. Robert McDonald	Starkville	MS
Dr. Lynn McEwan	Palmdale	CA
Dr. Chaim Mei-Tal	Northridge	CA
Dr. Dawn Metzger	Denver	CO
Dr. Kim Michels	Kenner	LA
Dr. Don Miller	San Antonio	TX
Dr. John Moffa	Aberdeen	MD
Dr. Susan Moon	Memphis	TN
Dr. David Moreman	Front Royal	VA
Dr. Jack Musgrave	New Port Richey	FL
Dr. Christine Myers	Middletown	OH
Dr. Vincent Obsitnik	Peachtree City	GA

Investigator Name	City	State
Dr. Caroline O'Dair	Rancho Palos Verdes	CA
Dr. Pamela Ogden	Eau Claire	WI
Dr. Garret Okumura	Campbell	CA
Dr. Dale Olm	Benicia	CA
Dr. Jacqueline Ordronneau	Seattle	WA
Dr. Vern Otte, Dr. Cheryl Jones	Leawood	KS
Dr. Dennis Ovitsky	Pittsfield	MA
Dr. Gerianne Pandolfi	Wilmington	NC
Dr. L. Scott Papas	Canton	OH
Dr. David Payne	Santa Paula	CA
Dr. Roger Peduzzi	Hudson	MA
Dr. Doug Peterson	Bowling Green	KY
Dr. Nancy Peterson	Des Moines	IA
Dr. Sarah Pratt	Sedgwick	KS
Dr. Bridget Quatmann	Roanoke	VA
Dr. Richard Reiersen	Champlin	MN
Dr. Pamela Richard	Prospect	CT
Dr. Eileen Rowan	Bayville	NY
Dr. Gretchen Rowe	Inver Grove Heights	MN
Dr. Tracy Royer	Farmington	MO
Dr. Frederick Ruhl	Oak Creek	WI
Dr. Holly Samko	Greenwood	IN
Dr. Robert Schladetzky	Port Hadlock	WA
Dr. Ralph Schoemann	Guilford	CT
Dr. Alice Schottenstein	Chagrin Falls	OH
Dr. Alan Schreier	Pleasantville	NY
Dr. Kate Schulze-Kellman	Tucson	AZ
Dr. Bruce Silverman	West Hollywood	CA
Dr. Jim Smith	Gallway	NY
Dr. Richard Smits	Fort Wayne	IN
Dr. Jeff Solomon	Terre Haute	IN
Dr. Katy Sommers	Ukiah	CA
Dr. Ted Staph	Plano	TX
Dr. William Stehnach	Saint Louis	MO
Dr. Bruce Steinfeldt	La Belle	FL
Dr. Suzie Steinhauser	Gualala	CA
Dr. Linda Stevelt	North Wood	OH
Dr. Ira Stone	Watertown	CT
Dr. Kevin Stoothoff	Ocala	FL
Dr. Terri Summers	Woodbridge	VA
Dr. Richard Thoma	Cheektowaga	NY
Dr. Karen Thomas	Riverdale	GA
Dr. Mark Thompson	Columbia	MO

Investigator Name	City	State
Dr. Teresa Tomchick	Issaquah	WA
Dr. David Visser	South Bend	IN
Dr. Dan Walker	Dallas	TX
Dr. Susan Weinstein	Little Rock	AR
Dr. Mary Welle	Urbana	IL
Dr. Dennis White	Tecumseh	MI
Dr. Mary Wictor	Duluth	MN
Dr. Katharine Wilderoter	Sarver	PA
Dr. Jeffrey Williams	Jamestown	PA
Dr. Michael Williams	Scottsdale	AZ
Dr. Gail Wolfe	Okemos	MI
Dr. Craig Zabel	Sugar Grove	IL
Dr. Patricia Ziegler	Springfield	MO

Veterinary Behavioral Consultant Investigators:

Benjamin L Hart, DVM, ACVB (chief behavioral investigator)
Professor of Physiology and Behavior
School of Veterinary Medicine
University of California at Davis
Davis, CA 95616

Kelly D. Cliff, DVM
Staff Research Associate
School of Veterinary Medicine
University of California at Davis
Davis, CA 95616

Ilana Reisner, DVM, ACVB
Veterinary Behavioral Consultations
PO Box 105
Brooktondale, NY 14817

Lisa Darling, DVM
Private Consultant
Kearney, MO 64060

Heidi Ball, DVM
Private Consultant
Davis California, 95616

Purpose: 1) To assess the efficacy of Anipryl® administered orally once daily for control of clinical signs associated with CDS and 2) To evaluate the clinical safety of Anipryl® in dogs.

Animals: 199 client-owned dogs (82 males and 117 females) of various breeds with acquired cognitive dysfunction were enrolled. The dogs ranged in age from 7 to 20 years (mean = 13.9 years) and weighed between 4.5 and 152 pounds (mean = 36.7 pounds).

Control: During the first 4 week phase, one group received placebo tablets comprised of the formulation excipients without active ingredient. The placebo tablets were indistinguishable from Anipryl® tablets.

Enrollment: Each dog enrolled met the following criteria:

- 1) Presence of acquired cognitive dysfunction, as documented by the presence of at least 3 of the following cognitive problems: disorientation; decreased activity; increased sleep or changes in sleep/wake cycle; loss of housetraining or reduced signaling behavior (i.e, signals less to go outside); decreased enthusiasm of greeting behavior; decreased responsiveness to attention.
 - 2) Age 10 years or older; giant breed dogs, age 7 years or older.
 - 3) No known concurrent debilitating disease that would preclude monitoring response to therapy.
 - 4) No concurrent treatment or recent treatment with corticosteroids or other medication that could cause polyuria/polydipsia or substantially affect behavior.
 - 5) No concurrent treatment with medications known to interact with Anipryl®.
- Dogs were excluded if they had evidence of concurrent disease or concurrent drug therapy that could preclude monitoring of response to therapy, or if they had other behavioral problems such as aggression.

Dosage form: Anipryl® formulated into 2 mg, 5 mg, and 15 mg tablets

Route of administration: Oral

Dosage: 0 mg/kg administered to one group of 67 dogs, 0.2 mg/kg administered to one group of 65 dogs, and 1.0 mg/kg administered to one group of 67 dogs once daily in the morning.

Study Duration: Three months, divided into two phases.

- | | |
|----------|--|
| Phase 1: | Three dose groups (placebo, 0.2 mg/kg, or 1.0 mg/kg) were studied for 4 weeks. |
| Phase 2: | All dogs were administered 1.0 mg/kg of Anipryl® in open label fashion for 8 additional weeks. |

Variables evaluated: Entrance and post-treatment evaluation criteria consisted of evaluation of the following behaviors: orientation, activity, sleep pattern, housetraining, responsiveness, and greeting behavior. The owner stated if each behavior had worsened, stayed the same, or improved. The owners' assessments of changes in behavior were obtained by telephone interview with the veterinary behavioral consultants at enrollment, week 4 and week 12.

Results: Phase 1-(4-week, placebo controlled dose range study):

Results of the 4-week study are based on 181 evaluable dogs. Table 1 shows proportions of dogs that improved following 4 weeks of treatment with Anipryl® or placebo. Improvement of individual parameters was evaluated in those dogs with the behavioral abnormality in question at the initiation of the study. Significant improvements were observed in sleep pattern, housetraining and activity.

Table 1. Proportion of Improved Dogs at Week 4 by Dose Group

Behavior (Number affected at enrollment)	Control	0.2 mg/kg	1.0 mg/kg	Overall p-value*
Orientation (179)	22/62 (35.5%)	24/59 (40.7%)	32/58 (55.2%)	0.098
Activity (166)	16/56 (28.6%)	22/57 (38.6%)	29/53 (54.7%)	0.012
Sleep (164)	9/54 (16.7%)	17/55 (30.9%)	29/55 (52.7%)	0.001
Responsiveness (158)	23/55 (41.8%)	26/55 (47.3%)	25/48 (52.1%)	0.499
Housetraining (157)	15/57 (26.3%)	21/54 (38.9%)	16/46 (34.8%)	0.030
Greeting (145)	12/48 (25.0%)	20/51 (39.2%)	15/46 (32.6%)	0.584

*For the Cochran-Mantel-Haenszel test for nonzero correlation, indicating increased improvement with increasing dose.

Phase 2- (Open label dose confirmation study, continued to week 12):

Results of the 8-week open label phase of the study are based on 157 evaluable dogs. Analyses of week 12 evaluations compared the percent improvement at 12 weeks to that observed at 4 weeks of treatment. Table 2 results indicate some dogs that did not improve by week 4 showed improvement by week 12. This tendency to improve was observed in all 3 treatment groups by 12 weeks of treatment regardless of the initial treatment received during the first 4 week period (i.e. placebo, 0.2, or 1.0 mg/kg of Anipryl®), indicating that some increased improvement may be seen with extended use, even among high dose (1.0 mg/kg) group animals. Significant improvement occurred in activity, sleep pattern, and housetraining.

Table 2. Proportion of Improved Dogs at Week 12 Among Those Not Improved at Week 4

The headings for the proportions below refer to the dosage groups the dogs were in during the first phase of the trial. In phase 2, all dogs received 1.0 mg/kg.

Behavior (n)	Control	0.2 mg/kg	1.0 mg/kg
Orientation (86)	17/35 (48.6%)	18/29 (62.1%)	11/22 (50.0%)
Activity (83)	15/35 (42.9%)	15/31 (48.4%)	6/17 (35.3%)
Sleep (96)	12/41 (29.3%)	12/35 (34.3%)	6/20 (30.0%)
Responsiveness (68)	14/27 (51.8%)	12/24 (50.0%)	8/17 (47.1%)
Housetraining (90)	12/36 (33.3%)	18/29 (62.1%)	13/25 (37.1%)
Greeting (82)	7/32 (21.9%)	10/27 (37.0%)	8/23 (34.8%)

To assess the duration of effect, the change between week 4 and week 12 among those dogs who were evaluated as improved at week 4 was evaluated. The proportion of dogs that regressed at week 12 among those improved at week 4 was fairly consistent across the groups. The duration of effect may be as short as 8 weeks in about 50% of the cases.

Conclusions: In this clinical trial, Anipryl® administered at 1.0 mg/kg once daily was shown to provide safe and effective control of clinical signs associated with CDS in pet dogs. The onset, duration and magnitude of response varied with individual dogs. Based on the results in Table 1, trends indicate that the higher dose of 1.0 mg/kg is more effective than the lower dose of 0.2 mg/kg.

Adverse Reactions: Refer to the Safety section (page 12) for adverse events observed in clinical trials.

CD3, Multi-Site Clinical Trial of Anipryl® for Canine Cognitive Dysfunction

Type of study: Open label, multi-site dose confirmation clinical trial

Investigators:

Investigator Name	City	State
Dr. W.A. Andrews	Bonner Springs	KS
Dr. Ward Brown	Kansas City	MO
Dr. Don Dinges	Leawood	KS
Dr. Rusty Erickson, Dr. Todd Goodman	Mission	KS
Dr. Karen Eyer-Stokes	Overland Park	KS
Dr. Wayne Hunthausen,	Westwood	KS
Dr. Annette Frerking		
Dr. Kevin Lesslie	Shawnee	KS
Dr. Scott Lichlyter	Brentwood	CA
Dr. Keven McShane,	Austin	TX
Dr. R. Brenton Smith		
Dr. Vern Otte, Dr. Cheryl Jones,	Leawood	KS
Dr. Keith Longhofer		
Dr. Dan Reimer, Dr. Mary Haitt	Sepulveda	CA
Dr. Brian Rind	Great Neck	NY
Dr. Jill Sandler	Overland Park	KS
Dr. Tom Shackelford	Carmel	IN
Dr. David Theiss	Lee's Summit	MO
Dr. Steve White, Dr. Scott Mickleson	Fairway	KS
Dr. Jarvis Williams, Dr. Sandi Leonard	Kansas City	MO

Purpose: The objectives of this clinical trial were to assess the efficacy and safety of Anipryl® for CDS in the dog.

Animals: 73 client-owned dogs (29 males and 44 females) of various breeds with spontaneously occurring CDS were enrolled. The dogs ranged in age from 7 to 19 years (mean = 15 years) and weighed between 8 and 80 pounds (mean = 31 pounds).

Controls: Each animal served as its own control.

Diagnosis: Diagnosis of CDS was based on the presence of one or more of the following clinical or behavioral signs: decreased appetite, decreased awareness of surroundings, decreased ability to recognize familiar places, people or other animals, decreased hearing, decreased ability to climb up and down stairs, decreased tolerance to being alone, development of compulsive behavior or repetitive behaviors or habits, circling, tremors or shaking, disorientation, decreased activity level, abnormal sleep wake cycles, loss of house training, decreased or altered responsiveness to family members, and decreased or altered greeting behavior. Dogs were excluded if they had evidence of concurrent disease or concurrent drug therapy that could preclude monitoring of response to therapy, or if they had other behavioral problems such as aggression.

Dosage form: Anipryl® formulated into 2 mg, 5 mg, and 15 mg tablets

Route of administration: Oral

Dosage: One dose group was studied: dogs received 0.5 mg/kg orally once daily throughout the trial. Three dogs had an increase in dose to 1.0 mg/kg because of lack of efficacy and two dogs had the dosage halved due to adverse events (hyperactivity).

Study Duration: Three months.

Variable evaluated: Changes in the behaviors and clinical signs listed below in Table 3.

Results: To determine responses to 0.5 mg/kg once daily Anipryl® treatment, individual parameters were evaluated in this trial by methods similar to those used in the CD/HT clinical trial. A complete listing of response to individual parameters is displayed in Table 3. The sleep pattern improvement is consistent with the dose response pattern observed for this variable in the CD/HT study. The improvement rates for housetraining, activity, and orientation exceed that observed in 1.0 mg/kg dose group from the CD/HT study.

Table 3. Proportion Improved at 4 Weeks

Parameters in bold are the same parameters evaluated in CD/HT clinical trial.

Behavior	Proportion* (%)
Housetraining	19/47 (40.4%)
Activity/attention	30/51 (58.8%)
Orientation/awareness	28/47 (59.6%)
Recognition	15/41 (36.6%)
Tolerance to being alone	4/31 (12.9%)
Circling	8/20 (40.0%)
Sleep/wake	13/46 (28.3%)
Whining/whimpering	10/29 (34.5%)
Alertness	31/55 (56.4%)
Response to commands	12/60 (20.0%)
Recognizing people	11/46 (23.9%)
Memory	11/50 (22.0%)
Learning ability	3/50 (6.0%)
Interact with people	12/42 (28.6%)
Interact with other dogs	7/47 (14.9%)

*The proportions are the number improved over the number with the problem at the beginning of the study.

Conclusions: The results of this clinical trial support the inclusion of 0.5 mg/kg as the lower end of a dosage range.

5. Safety:

The safety of Anipryl® is based on data in the original approval (refer to the Freedom of Information Summary dated May 30, 1997). The information below describes the adverse events reported in the CDS clinical field trials.

In the CD/HT clinical trial, 132 dogs were monitored for adverse events while on Anipryl® for up to 12 weeks and 67 dogs were monitored on the drug for up to 8 weeks. In the CD3 trial, 73 dogs were monitored while on Anipryl® for up to 12 weeks.

The following table lists the adverse reactions reported in the 2 clinical trials. The 67 dogs that received placebo during Phase 1 of the CD/HT trial are included.

Table 4: Adverse events from 2 clinical field trials

Adverse Event	Placebo (n=67)	Anipryl® (n=272)
vomiting	14 (21%)	87 (32%)
diarrhea	7 (10%)	55 (20%)
hyperactive/restless*	4 (6%)	42 (15%)
anorexia	1 (1%)	29 (11%)
neurologic**	1 (1%)	26 (10%)
lethargy	1 (1%)	20 (7%)
urinary tract infection	1 (1%)	17 (6%)
salivation	3 (4%)	15 (6%)
weakness	0 (0%)	15 (6%)
pale gums	1 (1%)	14 (5%)
polyuria/polydipsia	1 (1%)	13 (5%)
pruritis/dermatologic	1 (1%)	13 (5%)
weight loss	0 (0%)	12 (4%)
panting	1 (1%)	10 (4%)
cardiovascular/resp***	0 (0%)	10 (4%)
diminished hearing	0 (0%)	7 (3%)

*includes hyperactive, irritable, anxious, restless, abnormal repetitive movements

**includes ataxia, incoordination, staggering, disorientation, decreased proprioception, seizure

***includes heart murmurs, tachycardia, collapse, dyspnea, pleural effusion, sneezing

In the CD/HT trial, 5 dogs had the drug discontinued because of the following adverse events: 1) vomiting and diarrhea, 2) hyperactivity, 3) increase in destructive behavior associated with separation anxiety, 4) anemia, and 5) stiffness and polydipsia.

In the CD3 trial, 2 dogs had the dosage halved because they became too active and 5 dogs had the drug discontinued because of the following adverse events: 1) vomiting (in 2 dogs); 2) agitation, 3) stargazing and trembling a few hours after the first tablet was given, and 4) possible drug interaction. After being on the drug for about a week one dog experienced weakness, confusion, incoordination and “seizure-like” activity. The dog was also on metronidazole, prednisone, and trimethoprim sulfa. All drugs were discontinued, and the dog returned to normal.

A trend in hematocrit levels was noticed during review of individual case reports. Some dogs experienced a drop in hematocrit during the clinical trials. The decreases seen were usually within the normal range and not accompanied by any clinical signs.

One dog had a rapid drop below the normal range accompanied by lethargy and anorexia. The dog recovered after the drug was discontinued.

6. Human Safety:

Human Safety Relative to Food Consumption: Data on human safety, pertaining to consumption of drug residues in food, were not required. This drug is to be labeled for use in dogs, which are non-food animals.

Human Safety Relative to Possession, Handling and Administration: Labeling contains an adequate caution statement. Labeling states: "Keep out of reach of children."

7. Agency Conclusions:

The data in support of this NADA comply with the requirements of Section 512 of the Act and Section 514.111 of the implementing regulations. The data demonstrate that Anipryl® (selegiline hydrochloride, L-deprenyl), when used under labeled conditions of use, is safe and effective.

Under section 512(c)(2)(F)(iii) of the FFDCA, this approval for non food producing animals qualifies for THREE years of marketing exclusivity beginning on the date of approval because the application contains substantial evidence of the effectiveness of the drug involved, or studies of animal safety required for the approval of the application conducted or sponsored by the applicant.

The drug is restricted for use by or on the order of a licensed veterinarian because professional expertise is required for the diagnosis of clinical signs associated with cognitive dysfunction syndrome and for the monitoring of adverse events and response to therapy.

Patent information: The sponsor holds the following patents: 5,225,446 (expires 8-31-10); 5,276,057 (expires 1-4-11); 5,387,615 (expires 2-7-12); 5,565,495 (expires 10-15-13); 5,561,163 (expires 10-1-13); 5,151,449 (expires 8-31-10); and 5,192,808 (expires 8-31-10).

8. Labeling (attached):

Package Insert

Cartons for 2, 5, 10, 15 and 30 mg tablets

Blister package foil backing for 2, 5, 10, 15 and 30 mg tablets

ANIPRYL®

(selegiline hydrochloride,
L-deprenyl hydrochloride)

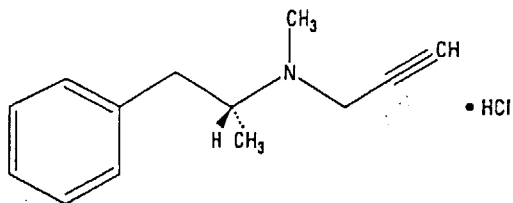
Tablets

For use in dogs only

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Anipryl (selegiline hydrochloride) tablets are white, convex tablets containing 2, 5, 10, 15, and 30 mg of selegiline HCl. It is commonly referred to in the clinical and pharmacological literature as L-deprenyl (the levorotatory form of deprenyl HCl).

Selegiline hydrochloride is (—)-(R)-N,α-Dimethyl-N-2-propynyl-phenethylamine hydrochloride.



Molecular Formula: C₁₃H₁₇N HCl
Molecular Weight: 223.75

PHARMACOLOGY: Selegiline is an irreversible inhibitor of monoamine oxidase (MAO).^{1,2} MAOs are widely distributed throughout the body and are subclassified into 2 types, A and B, which differ in their substrate specificity and tissue distribution. Selegiline is believed to be a selective inhibitor of MAO-B at recommended dosages in the dog due to its greater affinity for type B enzyme active sites compared to type A sites.¹ In CNS neurons, MAO plays a role in the catabolism of catecholamines, (dopamine, and, to a lesser extent, norepinephrine and epinephrine) and serotonin.^{1,2} Selegiline may have pharmacologic effects unrelated to MAO-B inhibition. There is some evidence that it may increase dopaminergic activity by other mechanisms, including increasing synthesis and release of dopamine into the synapse as well as interfering with dopamine re-uptake from the synapse.²⁻⁴ Effects resulting from selegiline administration may also be mediated through its metabolites. Two of its 3 principal metabolites, L-amphetamine and L-methamphetamine, have pharmacologic actions of their own. However, the extent to which these metabolites contribute to the effects of selegiline are unknown.

Therapeutic effects of selegiline are thought to result in part from enhanced catecholaminergic nerve function and increased dopamine levels in the CNS.^{5,6} The pathogenesis of the development of clinical signs associated with cognitive decline is considered to be partly a result of a decrease in the level of catecholamines in the CNS and deficiencies in neurotransmission.⁷ There is evidence which points to hypothalamic dopamine deficiency playing a role in the pathogenesis of pituitary dependent hyperadrenocorticism in the dog.^{8,9}

Based upon IV administration of selegiline to 4 mixed breed female dogs, the plasma elimination half-life was estimated to be 60 ± 10 minutes (mean ± SD) and the volume of distribution at steady-state (V_{ss}) was estimated to be 9.4 ± 1.6 L/kg (mean ± SD). The relatively large V_{ss} suggests that the selegiline is extensively distributed to body tissues. The absolute bioavailability, F, of an oral solution was less than 10%.¹⁰

INDICATIONS: Anipryl tablets are indicated for the control of clinical signs associated with canine cognitive dysfunction syndrome (CDS) and control of clinical signs associated with uncomplicated canine pituitary dependent hyperadrenocorticism (PDH).

CONTRAINDICATIONS: Anipryl is contraindicated in patients with known hypersensitivity to this drug.

In humans, selegiline is contraindicated for use with meperidine and this contraindication is often extended to other opioids.

WARNINGS: Keep out of reach of children. Not for human use.

Anipryl should not be administered at doses exceeding those recommended (0.5–2.0 mg/kg once daily).

In humans, concurrent use of MAO inhibitors with alpha-2 agonists has resulted in extreme fluctuations of blood pressure; therefore, blood pressure monitoring is recommended with concurrent use in dogs. Also, in humans, severe CNS toxicity including death has been reported with the combination of selegiline and tricyclic antidepressants, and selegiline and selective serotonin reuptake inhibitors. Although no such adverse drug interactions were reported in the clinical trials in dogs, it seems prudent to avoid the combination of Anipryl and selective serotonin reuptake inhibitors (e.g., fluoxetine) as well as Anipryl and tricyclic (e.g., clomipramine, amitriptyline, imipramine) or other antidepressants.

At least 14 days should elapse between discontinuation of Anipryl and initiation of treatment with a tricyclic antidepressant or selective serotonin reuptake inhibitor. Because of the long half-life of fluoxetine and its active metabolites, at least 5 weeks should elapse between discontinuation of fluoxetine and initiation of treatment with Anipryl.

Concurrent use of Anipryl with ephedrine or potential MAO inhibitors, such as amitraz, is not recommended.

PRECAUTIONS:

General: Anipryl is not recommended for other behavior prob-

lems such as aggression. In the clinical trials, 3 dogs showed an increase in aggression while on this drug. The safety and efficacy of Anipryl has not been evaluated in dogs with debilitating systemic diseases other than PDH.

The decision to prescribe Anipryl should take into consideration that the MAO system of enzymes is complex and incompletely understood and there is only a limited amount of carefully documented clinical experience with selegiline. Consequently, the full spectrum of possible responses to selegiline may not have been observed in pre-marketing evaluation of the drug. It is advisable, therefore, to observe patients carefully for atypical responses.

Endocrine function testing to confirm pituitary dependent hyperadrenocorticism should be performed prior to Anipryl administration for that condition. Anipryl is not recommended for treatment of patients with hyperadrenocorticism not of pituitary origin such as those due to an adrenal tumor or administration of glucocorticoids. If complications of PDH are evident at the time of diagnosis or emerge during Anipryl therapy, the patient should be evaluated and, if warranted, alternative therapy considered. Concurrent use of Anipryl in conjunction with other therapies of canine PDH has not been evaluated.

Laboratory Tests: No specific laboratory tests are deemed essential for the management of patients on Anipryl, as response to therapy should be based on the history and physical examinations for both PDH and CDS. In clinical trials for PDH, no correlation was found between an individual patient's clinical response and results of the low dose dexamethasone suppression (LDDS) test. There was no evidence of adrenal insufficiency in these trials.

In the 12 week clinical trial for CDS, a small number of dogs had a drop in hematocrit; some dropping within the normal range and some dropping below 37%. The clinical significance of this is unknown at this time. It is advisable to conduct a thorough physical examination and to consider appropriate laboratory tests to establish hematological and serum biochemical baseline data prior to administration of Anipryl.

Reproductive Safety: The safety of Anipryl in breeding, pregnant and lactating bitches, and breeding dogs has not been determined.

ADVERSE REACTIONS: In clinical trials, 404 dogs treated with Anipryl for as long as 18 months were monitored for the occurrence of adverse events. Many of the observations listed in the following table may be associated with the underlying disease (PDH or CDS), the advanced age of the patients or the development of unrelated concurrent disease. One index of relative importance, however, is whether or not a reaction caused treatment discontinuation. Eighteen dogs (4%) experienced one or more of the following adverse events that led either to discontinuation of therapy with Anipryl, dismissal from the study, or a reduction in dose: restlessness/agitation, vomiting, disorientation, diarrhea, diminished hearing, possible drug interaction (weakness, confusion, incoordination and "seizure-like" activity while being treated concurrently with metronidazole, prednisone, and trimethoprim sulfa), increase in destructive behavior in a dog with separation anxiety, anorexia, anemia, stiffness and polydipsia.

Percentage of Dogs with Adverse Events Reported in Clinical Field Trials

Adverse Event	Anipryl (n=404)	Placebo (n=67)
vomiting	26%	21%
diarrhea	18%	10%
hyperactive/restless*	12%	6%
anorexia	8%	1%
neurologic**	6%	1%
lethargy	6%	1%
salivation	5%	4%
urinary tract infection	4%	1%
pruritis/dermatologic	4%	1%
weakness	4%	0
pale gums	3%	1%
polyuria/polydipsia	3%	1%
weight loss	3%	0
diminished hearing	2%	0
panting	2%	1%
cardiovascular/respiratory***	2%	0
licking	2%	1%

*This includes hyperactivity, irritability, abnormal repetitive movements, anxiousness, and restlessness.

**This includes ataxia, incoordination, staggering, disorientation, decreased proprioception, and seizure.

***This includes heart murmurs, tachycardia, collapse, dyspnea, pleural effusion, and sneezing.

DOSAGE AND ADMINISTRATION:

CDS: The recommended dosage for oral administration for the control of clinical signs associated with CDS is 0.5–1.0 mg/kg once daily, preferably administered in the morning. Initially, dogs should be dosed to the nearest whole tablet. Adjustments should then be made based on response and tolerance to the drug.

PDH: The recommended dosage for the control of clinical signs associated with canine PDH is 1.0 mg/kg once daily, preferably administered in the morning. If no improvement is observed after 2 months of therapy, dosage may be increased to a maximum of 2.0 mg/kg once daily. If no improvement is seen after 1 month at the higher dose or if at any time clinical signs progress, the dog should be re-evaluated. In dogs whose clinical signs of PDH progress despite Anipryl therapy in the absence of concurrent disease, alternate therapy should be considered.

Dogs should be monitored closely for possible adverse events associated with any increase in dose.

Clinical Use of Anipryl in CDS: CDS is an age-related deterioration of cognitive abilities characterized by behavioral changes not wholly attributable to a general medical condition such as neoplasia, infection, or organ failure. CDS is typified by multiple cognitive impairments which affect the dog's function. In clinical trials, the observed behavioral changes associated with CDS in older dogs included: disorientation, decreased activity level, abnormal sleep/wake cycles, loss of housetraining, decreased or altered responsiveness to family members; and decreased or altered greeting behavior. In clinical trials, Anipryl was shown to be effective in controlling clinical signs associated with CDS. After 4 weeks of treatment, dogs treated with Anipryl showed significant improvement when compared to placebo-treated controls

in sleeping patterns, housetraining, and activity level. Some dogs showed increased improvement up to 3 months, however, onset, duration and magnitude of response varied with individual dogs.

The diagnosis of CDS in dogs is a diagnosis of exclusion, based on thorough behavioral and medical histories, in conjunction with appropriate diagnostic work-up and testing.¹¹ Periodic patient monitoring to evaluate the response and tolerance to the drug and for the presence of concurrent or new disease is recommended.

Clinical Use of Anipryl in PDH: Clinical signs of PDH seen in clinical trials included panting, reduced activity, polydipsia, polyuria, changes in sleep patterns, altered appetite, obesity, alopecia, abdominal distention, reduced skin elasticity, thin skin, poor hair growth, pyoderma, decreased responsiveness to attention, and decreased enthusiasm of greeting. In clinical studies involving 125 evaluable cases of naturally occurring PDH, Anipryl was shown to be effective in controlling clinical signs associated with the disease. On physical examination, abdominal distention was the parameter which most consistently improved following treatment with Anipryl. Based on owner assessments, activity level was the parameter most consistently evaluated as "improved." Approximately 60% of the dogs were evaluated by the veterinarians and owners to be "slightly improved" to "improved" after 1 month of Anipryl therapy. By month 2, veterinarians reported that approximately 77% were "slightly improved" to "improved." Approximately 20% of dogs did not respond to Anipryl and were deemed treatment failures.

Those dogs that responded to Anipryl tended to do so within 1–2 months after treatment was initiated. Response to therapy varied between patients with some dogs showing improvement in all presenting clinical signs and others showing improvement in only 1–2 parameters. Duration of response was also variable, with some dogs continuing on Anipryl for over 1 year with good control of clinical signs and others showing an initial response to therapy only to be followed within several months by recurrence of clinical signs of PDH. There was no correlation demonstrated between an individual dog's clinical response to Anipryl and that dog's low dose dexamethasone suppression test results, therefore, monitoring should be based on history and physical examination findings.

SAFETY: In a laboratory safety study, Anipryl was administered orally to healthy adult beagles once daily for 6 months at doses of 0, 1, 2, 3, or 6 mg/kg (0.5x, 1x, 1.5x and 3x the maximum recommended daily dose of 2.0 mg/kg). The drug was demonstrated to be safe at the recommended dose range of 0.5–2.0 mg/kg. The following statistically significant clinical observations were noted in dogs in the 1.5x and 3x group: salivation, decreased pupillary response, and decreased body weight despite normal to increased feed consumption. Additional reactions seen at the 3x dose included panting, decreased skin elasticity (dehydration) and stereotypic behaviors, i.e., weaving (repetitive left to right movement) in the cage. This repetitive movement started several hours after dosing but was no longer present at the time of the next morning dose. There were no changes noted in blood pres-

sure, heart rate and ECG parameters, nor were there any ophthalmic changes.

REFERENCES:

1. Milgram NW, Ivy GO, Murphy MP, *et al*: Effects of chronic oral administration of L-deprenyl in the dog. *Pharmacol Biochem Behav* 51:421–428, 1995.
2. Heinonen EH, Lammintausta R: A review of the pharmacology of selegiline. *Acta Neurol Scand* 84(suppl. 136): 44–59, 1991.
3. Knoll J: R-(-)-Deprenyl (selegiline, Movergen®) facilitates the activity of the nigrostriatal dopaminergic neuron. *J Neural Transm* (suppl. 25):45–66, 1987.
4. Heikkilä RE, Cabbat FS, Manzino L, *et al*: Potentiation by deprenyl of l-dopa induced circling in nigral-lesioned rats. *Pharmacol Biochem Behav* 15:75–79, 1981.
5. Knoll J, Miklya I, Knoll B, *et al*: (-)-Deprenyl and (-)-1-phenyl-2-propylaminopentane, [(–) PPAP], act primarily as potent stimulants of action potential - transmitter release coupling in the catecholaminergic neurons. *Life Sci* 58:817–827, 1996.
6. Riederer P, Youdim MBH, Rausch WD, *et al*: On the mode of action of L-deprenyl in the human central nervous system. *J Neural Transm* 43:217–226, 1978.
7. Amsten, AFT: Catecholamine mechanisms in age-related cognitive decline. *Neurobiol Aging* 14:639–641, 1993.
8. Peterson ME, Palkovits M, Chiu CC, *et al*: Biogenic amine and corticotropin-releasing factor concentrations in hypothalamic paraventricular nucleus and biogenic amine levels in the median eminence of normal dogs, chronic dexamethasone-treated dogs, and dogs with naturally-occurring pituitary-dependent hyperadrenocorticism (Canine Cushing's Disease). *J Neuroendocrinology* 1:169–171, 1989.
9. Bruyette DS, Ruehl WW, Enriken TL, *et al*: Treating canine pituitary-dependent hyperadrenocorticism with L-deprenyl. *Veterinary Medicine* 92:711–727, 1997.
10. Mahmood I, Peters DK, Mason WD: The pharmacokinetics and absolute bioavailability of selegiline in the dog. *Biopharm Drug Dispos* 15:653–664, 1994.
11. Ruehl WW, Hart BL: Canine cognitive dysfunction, in Dodman N, Shuster L (eds): *Psychopharmacology of Animal Behavior Disorders*. Cambridge, MA, Blackwell Science, Inc. 1998.

HOW SUPPLIED: Five tablet strengths are available in blister packs of 30 tablets each: 2 mg, 5 mg, 10 mg, 15 mg, and 30 mg. Each box contains 1 blister pack (30 tablets).

STORAGE: Store at controlled room temperature 20°–25°C (68°–77°F).

For a copy of the Material Safety Data Sheet (MSDS) or to report adverse reactions call Pfizer Animal Health at 1-800-366-5288.



Distributed by:

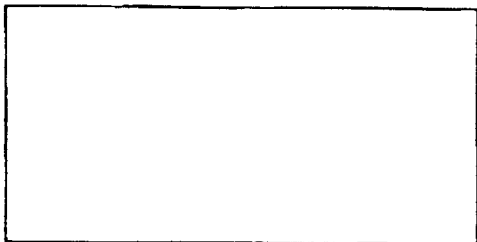
Animal Health

Exton, PA 19341, USA
Div. of Pfizer Inc
NY, NY 10017

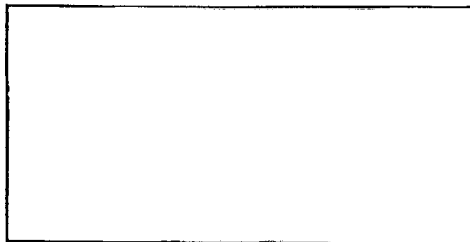
75-8191-02
November 1998
Printed in USA

Made in USA
9811 20-8191-02

Animal Health
Eaton, PA 15041, USA
Div. of Pfizer Inc.
NY, NY 10017
Distributed by:



Client



Client/Dosage Information

Each Anipryl tablet contains 2 mg of selegiline hydrochloride.
Indications: Anipryl tablets are indicated for the control of clinical signs associated with canine Cognitive Dysfunction Syndrome and control of clinical signs associated with uncomplicated canine Pituitary Dependent Hyperadrenocorticism.
Dosage and Administration: Cognitive Dysfunction Syndrome—Orally administer 0.5–1.0 mg/kg once daily, preferably in the morning. Pituitary Dependent Hyperadrenocorticism—Orally administer 1 mg/kg once daily, preferably in the morning.
See Package Insert for Complete Directions and Precautions
Store at Controlled Room Temperature 20°–25°C (68°–77°F)

ANIPRYL® 2mg 1 blister pack (30 tablets)

ANIPRYL® 2mg

ANIPRYL®
selegiline hydrochloride (L-deprenyl)



Tablets

For use in dogs only

Warnings: Keep out of reach of children. Not for human use.

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

1 blister pack (30 tablets)

2 mg

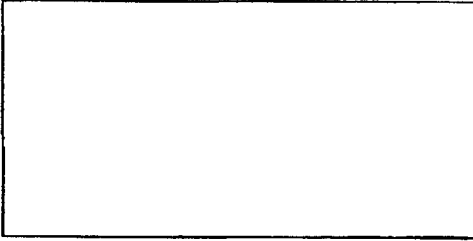
NADA #141-080, Approved by FDA



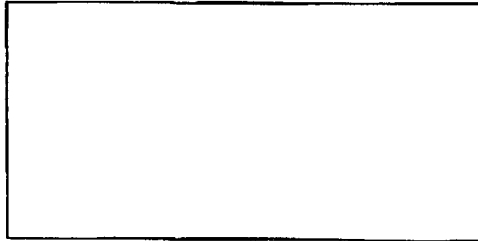
LOT XXXXXX EXP XXXX

Made in USA
9811 20-8192-02

Animal Health
Eli Lilly and Company
Greenfield, IN 46030, USA



Client



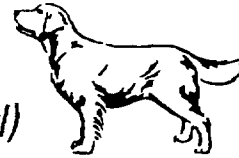
Client/Dosage Information

Each Anipryl tablet contains 5 mg of selegiline hydrochloride.
Indications: Anipryl tablets are indicated for the control of clinical signs associated with canine Cognitive Dysfunction Syndrome and control of clinical signs associated with uncomplicated canine Pituitary Dependent Hyperadrenocorticism.
Dosage and Administration: Cognitive Dysfunction Syndrome—Orally administer 0.5–1.0 mg/kg once daily, preferably in the morning. Pituitary Dependent Hyperadrenocorticism—Orally administer 1 mg/kg once daily, preferably in the morning.
See Package Insert for Complete Directions and Precautions.
Store at Controlled Room Temperature 20°–25°C (68°–77°F).

ANIPRYL® 5mg 1 blister pack (30 tablets)

ANIPRYL® 5mg

ANIPRYL®
selegiline hydrochloride (L-deprenyl)
Tablets



For use in dogs only

Warnings: Keep out of reach of children. Not for human use.

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

1 blister pack (30 tablets)

5mg

NADA #141-080, Approved by FDA



LOT XXXXXXXX EXP XXXX

9811 20-8193-02
Made in USA

Distributed by
Animal Health
Eli Lilly and Company
Div. of Pfizer Inc.
Kalamazoo, MI 49001



Clinic

Client/Dosage Information

Each Anipryl tablet contains 10 mg of selegiline hydrochloride.
Indications: Anipryl tablets are indicated for the control of clinical signs associated with canine Cognitive Dysfunction Syndrome and control of clinical signs associated with uncomplicated canine Pituitary Dependent Hyperadrenocorticism.
Dosage and Administration: Cognitive Dysfunction Syndrome—Orally administer 0.5–1.0 mg/kg once daily, preferably in the morning. Pituitary Dependent Hyperadrenocorticism—Orally administer 1 mg/kg once daily, preferably in the morning.
See Package Insert for Complete Directions and Precautions
Store at Controlled Room Temperature 20°–25°C (68°–77°F)

ANIPRYL® 10mg 1 blister pack (30 tablets)

ANIPRYL® 10mg

ANIPRYL®
selegiline hydrochloride (L-deprenyl)



Tablets

For use in dogs only

Warnings: Keep out of reach of children. Not for human use.

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

1 blister pack (30 tablets)

10 mg

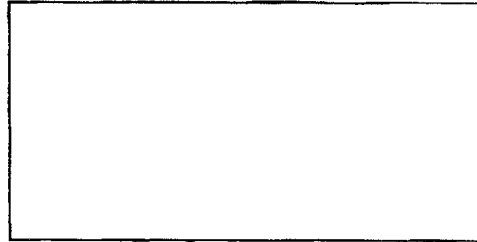
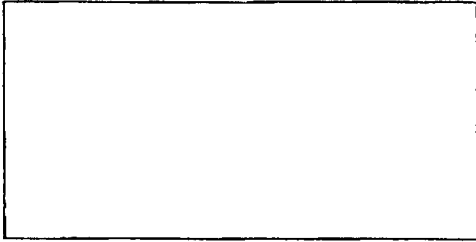
NADA #141-080, Approved by FDA



LOT XXXXXXXX EXP XXXX

Made in USA
9611 20-8194-02

Distributed by
Animal Health
Kenilworth, PA 19041, USA
Lilly, NY 10017



Clinic

Client/Dosage Information

Each Anipryl tablet contains 15 mg of selegiline hydrochloride.
Indications: Anipryl tablets are indicated for the control of clinical signs associated with canine Cognitive Dysfunction Syndrome and control of clinical signs associated with uncomplicated canine Pituitary Dependent Hyperadrenocorticism.
Dosage and Administration: Cognitive Dysfunction Syndrome—Orally administer 0.5–1.0 mg/kg once daily, preferably in the morning. Pituitary Dependent Hyperadrenocorticism—Orally administer 1 mg/kg once daily, preferably in the morning.
See Package Insert for Complete Directions and Precautions
Store at Controlled Room Temperature 20°–25°C (68°–77°F)

ANIPRYL® 15_{mg} 1 blister pack (30 tablets)

ANIPRYL® 15_{mg}

ANIPRYL®
selegiline hydrochloride (L-deprenyl)
Tablets



For use in dogs only

Warnings: Keep out of reach of children. Not for human use.

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

1 blister pack (30 tablets)

15_{mg}

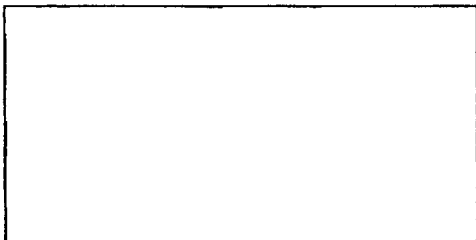
NADA #141-080, Approved by FDA



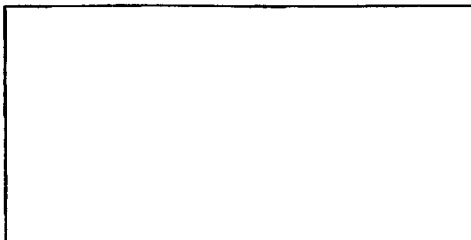
LOT XXXXXXXX EXP XXXX

Made in USA
9811 20-8195-02

Distributed by
Animal Health
Kroger, PA 19041, USA
Div. of Pfizer Inc
NY, NY 10017



Client



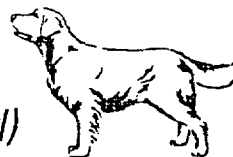
Client/Dosage Information

Each Anipryl tablet contains 30 mg of selegiline hydrochloride.
Indications: Anipryl tablets are indicated for the control of clinical signs associated with canine Cognitive Dysfunction Syndrome and control of clinical signs associated with uncomplicated canine Pituitary Dependent Hyperadrenocorticism.
Dosage and Administration: Cognitive Dysfunction Syndrome—Orally administer 0.5–1.0 mg/kg once daily, preferably in the morning. Pituitary Dependent Hyperadrenocorticism—Orally administer 1 mg/kg once daily, preferably in the morning.
See Package Insert for Complete Directions and Precautions
Store at Controlled Room Temperature 20°–25°C (68°–77°F)

ANIPRYL® 30mg 1 blister pack (30 tablets)

ANIPRYL® 30mg

ANIPRYL®
selegiline hydrochloride (L-deprenyl)



Tablets

For use in dogs only

Warnings: Keep out of reach of children. Not for human use.

Caution: Federal law restricts this drug to use by
or on the order of a licensed veterinarian.

1 blister pack (30 tablets)

30 mg

NADA #141-080, Approved by FDA



LOT XXXXXXXX EXP XXXX

Anipryl®
(selegiline HCl)

2 mg

[NADA #141-080,
Approved by FDA]
DIN 02184508
(Canada)

1 1/4" (W) x 1 3/16" (H)



Black

04-8191-02 5/07/98

Anipryl®

(selegiline HCl)

5 mg

[NADA #141-080,
Approved by FDA]

DIN 02184516
(Canada)

1 1/4" (W) x 1 3/16" (H)



Black

04-8192-02 5/07/98

Anipryl®
(selegiline HCl)

10 mg

[NADA #141-080,
Approved by FDA]
DIN 02229982
(Canada)

1 1/4" (W) x 1 3/16" (H)



Black

04-8193-02 5/07/98

Anipryl®

(selegiline HCl)

15 mg

[NADA #141-080,
Approved by FDA]

DIN 02184524
(Canada)

1 1/4" (W) x 1 3/16" (H)



Black

04-8194-02 5/07/98

Anipryl®

(selegiline HCl)

30 mg

[NADA #141-080,
Approved by FDA]

DIN 02229983
(Canada)

1 1/4" (W) x 1 3/16" (H)



Black

04-8195-02 5/07/98